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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/202,681	12/23/1999	ERIC J. MATHUR	09010/044001	3238

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EXAMINER

HUTSON, RICHARD G

ART UNIT	PAPER NUMBER
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1652

DATE MAILED: 04/23/2003

37

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/202,681

Applicant(s)

MATHUR ET AL.

Examiner

Richard G Hutson

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 17 January 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-11, 13-30 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) 1-11, 13 and 15-20 is/are allowed.
- 6) ☒ Claim(s) 22-30 is/are rejected.
- 7) ☒ Claim(s) 14 and 21 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

DETAILED ACTION

Applicants amendment of claims 3-5, 9, 10, 13 and 14-23 and addition of new claims 29 and 30, Paper No. 37, 1/17/2003, is acknowledged. Claims 1-11 and 13-30 are still at issue and are present for examination.

Applicants' arguments filed on 1/17/2003, Paper No. 37, have been fully considered and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Claim Objections

Claims 14 and 21 are objected to because of the following informalities:

Claims 14 and 21 are duplicative of claims 13 and 20, respectively.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 29 and 30, are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 29 and 30 are indefinite in that they are each confusing in that they are each drawn to the polynucleotide of claims 22 and 23, respectively, and claims 22 and 23 are each drawn to a "polynucleotide probe" that is described as they relate to specific polynucleotides. It is suggested that these claims be amended to clarify what is being claimed.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 22-28, 29 and 30 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The rejection is stated in the previous office actions, Paper No. 18, 8/14/2001, and Paper No. 36, 1/23/2003 as it applied to previous claims 3, 4, 6, 7, 8, 9, 13, 15-17, 20, 21 and 22-28. Applicants amendment of claims 3, 4, 6, 7, 8, 9, 13, 15-17, 20, 21 has resulted in these claims being withdrawn from this rejection. Applicants amendment of claims 22 and 23 has not resulted in the withdrawal of claims 22-28 from this rejection and the rejection is repeated below taking into account applicants amendment of claims 22 and 23.

Claims 22-28 are drawn to a polynucleotide probe comprising a nucleic acid sequence consisting of a sequence that hybridizes under stringent conditions to a

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polynucleotide encoding a polypeptide sequence of SEQ ID NO: 28, or a polypeptide having phosphatase activity and having at least 90% identity to the sequence of SEQ ID NO: 28, or a complement thereof.

The specification, however, only provides the representative species of claimed polynucleotides represented by SEQ ID NO: 19 and fragments thereof. There is no disclosure of any particular structure to function/activity relationship in the disclosed species. The specification also fails to describe additional representative species of these DNAs by any identifying structural characteristics or properties other than the characteristics recited in claims, for which no predictability of function is apparent.

The genus of DNAs that are claimed is a large variable genus with potentiality of encoding many different proteins. Therefore, many functionally unrelated DNAs are encompassed within the scope of these claims. The specification discloses the species encompassed by SEQ ID NO: 19 of the claimed genus which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus which reads on not only nucleic acids encoding all naturally occurring thermostable phosphatases, but also on mutant nucleic acids which encode proteins of undisclosed function. Therefore, one skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

Applicants have not traversed this rejection with respect to claims 22-28 in the previous response.

Newly added claims 29 and 30 are included in this rejection for the same reasons that the rejection of claims 22 and 23 is maintained.

Applicant is referred to the revised interim guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claims 22-28, 29 and 30 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for polynucleotides which encode the amino acid sequence of SEQ ID NO: 28 or enzymatically active fragments thereof, does not reasonably provide enablement for those polynucleotides which merely comprise a sequence that hybridizes under the specified stringent conditions to a polynucleotide that encodes the amino acids of SEQ ID NO: 28 or to a polypeptide having phosphatase activity and having at least 90% identity to the sequence of SEQ ID NO: 28, or a complement thereof.

The rejection is stated in the previous office actions, Paper No. 18, 8/14/2001, and Paper No. 36, 1/23/2003 as it applied to previous claims 3, 4, 6, 7, 8, 9, 13, 15-17, 20, 21 and 22-28. Applicants amendment of claims 3, 4, 6, 7, 8, 9, 13, 15-17, 20, 21 has resulted in these claims being withdrawn from this rejection. Applicants amendment of claims 22 and 23 has not resulted in the withdrawal of claims 22-28 from this rejection and the rejection is repeated below in part taking into account applicants amendment of claims 22 and 23.

Claims 22-28 are so broad as to encompass any polynucleotide comprising any nucleic acid sequence consisting of a sequence that hybridizes under the specified conditions to a polynucleotide encoding a polynucleotide encoding a polypeptide of

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SEQ ID NO: 28 or at least 90% identical to SEQ ID NO: 28 (claims 22-28). The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of polynucleotides broadly encompassed by the claims. The claims rejected under this section of U.S.C. 112, first paragraph, place minimal structural and no questionable functional limits on the claimed polynucleotides and polynucleotide probes. Since the nucleic acid sequence of a polynucleotide determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the polynucleotides' structure relates to its function. However, in this case the disclosure is limited to those polynucleotides that encode the phosphatase having the amino acid sequence of SEQ ID NO: 28.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass all modifications and fragments of any polynucleotide with the defined structural limitations, because the specification does not establish: (A) regions of the polynucleotide structure which may be modified without its functional activity; (B) the general tolerance of the claimed polynucleotides to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any nucleic acid residue of the polynucleotide with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful. Because of this lack of guidance, the extended experimentation that would be required to determine which substitutions would be acceptable to retain the desired function and the fact that the relationship between the sequence of a peptide and its tertiary structure (i.e. its activity) are not well understood and are not predictable (e.g., see Ngo et al. in *The Protein Folding Problem and Tertiary Structure Prediction*, 1994, Merz et al. (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495, Ref: U, Form-892), it would require undue experimentation for one skilled in the art to arrive at the majority of those polynucleotides of the claimed genus.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any number of nucleic acid modifications of any polynucleotide. The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of having the desired biological characteristics is

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unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir, 1988).

Applicants arguments as they relate to the above rejected claims are based on applicants assertion that they have provided structure (the sequence) and a functional limit, a probe that can be used to hybridize under specified conditions to a polynucleotide that encodes a polypeptide that has phosphatase activity. Applicants further argue that those polynucleotides that do not have the proper function or physical/chemical properties are not being claimed in the present invention. This argument is not found persuasive because those functions that are encompassed by applicants asserted functional limitation of claims 22-28, a "probe", remain unclear, such that this in combination with the structural limitation of a polynucleotide comprising a specified sequence remain un-enabled.

Newly added claims 29 and 30 are included in this rejection for the same reasons that the rejection of claims 22 and 23 is maintained.

The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir, 1988).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --
(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Claims 22-28, 29 and 30 are rejected under 35 U.S.C. 102(e) as being anticipated by Hirschberg et al. (U.S. Patent No: 5,792,903).

The rejection is stated in the previous office action.

Applicants traverse this rejection on the basis that there is no teaching in Hirschberg et al. that would indicate to one of ordinary skill in the art that the Hirschberg et al. 4928 base pair sequence would be desirable as a probe for a polynucleotide that encodes a polypeptide and moreover Hirschberg et al. does not teach a polynucleotide probe wherein the nucleic acid sequence consists of a sequence that hybridizes to a polynucleotide encoding a polypeptide having phosphatase activity. This argument is not found persuasive, while it is pointed out by applicants Hirschberg et al does not indicate to one of ordinary skill in the art that the Hirschberg et al. 4928 base pair sequence would be desirable as a probe for a polynucleotide that encodes a polypeptide, applicant is reminded that this is a anticipation rejection , not a rejection based on obviousness, and thus such a motivation is unnecessary. In contrast to applicants assertion, while Hirschberg et al. does not teach a polynucleotide probe wherein the nucleic acid sequence consists of a sequence that hybridizes to a polynucleotide encoding a polypeptide having phosphatase activity, Hirschberg et al. does teach a polynucleotide probe **comprising a** nucleic acid sequence consisting of a

sequence that hybridizes to a polynucleotide encoding a polypeptide having phosphatase activity (i.e. the previously referred to 17 contiguous nucleotides that are 100% identical between Hirschberg et al. and instantly disclosed SEQ ID NO: 19).

Newly added claims 29 and 30 are included in this rejection for the same reasons that the rejection of claims 22-28 is maintained, as Hirschberg et al. further teach vectors or plasmids as a part of the taught polynucleotides.

Thus claims 22-30 remain are rejected by Hirschberg et al.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Richard G Hutson whose telephone number is (703) 308-0066. The examiner can normally be reached on 7:30 am to 4:00 pm, M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on (703) 308-3804. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 305-3014 for regular communications and (703) 305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

A handwritten signature in black ink, appearing to read 'Richard Hutson', with a long horizontal line extending to the right.

Richard Hutson, Ph.D.
Primary Patent Examiner
Art Unit 1652
April 18, 2003